REMARKS

In the Office Action mailed March 3, 2004, the Examiner maintained the rejection of claims 48, 49, 51-53, and 55 under 35 U.S.C. § 103(a) and newly rejected claims 58 and 59 under 35 U.S.C. § 112, first paragraph, for lack of written description. The specific grounds for objection, and Applicant's response thereto, are set out in detail below.

Rejection under § 112, first paragraph

Claims 58 and 59 are rejected under 35 U.S.C. § 112, first paragraph, because the specification lacks deposit information for the hybridoma cell line producing MN-14 and WI2. Applicant respectfully traverse.

The sequences of the murine and humanized MN-14 antibody were publicly available via U.S. Pat. No. 5,874,540, issued on February 23, 1999, and the sequences of the murine and humanized WI2 antibody were publicly available via PCT Pub. No. WO97/34636, published on September 25, 1997. Accordingly, the sequences of MN-14 and WI2 sequences were publicly available at the filing date of this application and no deposit is required. Applicant submits that the rejection is inappropriate. Accordingly, withdrawal of the rejection respectfully is requested.

Rejection under § 103

Claims 48, 49, 51-53, and 55 are rejected under 35 U.S.C. § 103(a) as obvious over Eshhar *et al.*, Proc. Nat'l Acad. Sci. USA 90: 720 (1993) ("Eshhar"), WO 92/15322, Wagner *et al.*, Biotech. Therap. 3: 81 (1992) ("Wagner"), and applicant's purported "admission" at page 22 of the specification, in view of Hansen *et al.*, Cancer 71: 3478 (1993) ("Hansen"). Applicant acknowledges the Examiner's removal of claims 58 and 59 from the previous § 103(a) rejection and the removal of the Losman reference. Applicant respectfully traverses the maintained rejection.

The pending claims are directed to a method of inducing a cellular immune response against a tumor that expresses CEA by administering transfected T cells and then at least one cytokine. The present invention specifically achieves this response in one of two ways:

Firstly, (1) transfected T cells are administered in an effective immunostimulatory amount and are produced by obtaining T cells from the patient and transfecting these T cells with an expression vector containing a DNA molecule encoding either a chimeric immunoglobulin/T cell receptor or a chimeric immunoglobulin/CD3 protein, and where the immunoglobulin-encoding portion of the DNA molecule encodes the variable region of an antibody that binds with a Class III anti-CEA antibody, and further where the variable regions of the a and b polypeptide chains of the T cell receptor are replaced by the variable regions of this antibody; and then (2) at least one cytokine is administered.

Secondly, (1) transfected T cells are administered in an effective immunostimulatory amount and are produced by obtaining T cells from the patient and transfecting these T cells with an expression vector containing a DNA molecule encoding either a chimeric immunoglobulin/T cell receptor or a chimeric immunoglobulin/CD3 protein, and where the immunoglobulin-encoding portion of the DNA molecule encodes the variable region of an anti-idiotypic antibody that recognizes a Class III anti-CEA antibody, and further where the variable regions of the a and b polypeptide chains of said T cell receptor are replaced by the variable regions of this antibody; and then (2) at least one cytokine is administered.

The Examiner has previously admitted that the primary reference, Eshhar, fails to teach or suggest a specific showing that the chimeric gene can be used in adoptive immunotherapy, a specific showing that the immunoglobulin can be used to recognize a TAA or a disease caused by an infectious agent and the use of cytokines and/or administration of an anti-Id and the specific use of CEA. However, the Examiner

maintains that the teachings of secondary references provide the teachings missing from Eshhar. Applicant respectfully disagrees.

In response to Applicant's submission that it would not have been obvious to substitute the chimeric genes encoding the variable region of a Class III anti-CEA antibody or chimeric genes encoding the variable region of an anti-idiotypic antibody that recognizes a Class III anti-CEA antibody in adoptive immunotherapy as disclosed in Eshhar, the Examiner asserts that in view of Hansen there is no confusion in the art as to the Class III anti-CEA antibodies. However, the Examiner fails to acknowledge the references of Motomu Kuroki (Appendix 1 to February 6, 2004 response), Irvine (Appendix 2 to February 6, 2004 response) and Chen *et al.*, (Appendix 3 to February 6, 2004 response). These three references clearly evidence the confusion that existed at applicant's filing date with regard to the classification of CEA and its related family members. The Examiner cannot selectively pick out a single reference and assert that this reference clarifies the confusion present in the art. By doing so, the Examiner employs impermissible hindsight improperly based on Applicant's own specification.

In response to Applicant's submission that none of the cited prior art publications used in the Examiner's § 103 rejection disclose administering a cytokine subsequent to the administration of the transfected T cells containing the DNA encoding the variable region of a Class III anti-CEA antibody or the DNA encoding the variable region of an anti-idiotypic antibody that recognizes a Class III anti-CEA antibody, the Examiner asserts that the page 22 of the specification teaches the routine administration of cytokines to further an immune response. Nowhere in Applicant's specification is there any teaching or suggestion that it was routine to one of skill in the art to administering a cytokine subsequent to the administration of the transfected T cells containing the DNA encoding the variable region of a Class III anti-CEA antibody or the DNA encoding the variable region of an anti-idiotypic antibody that recognizes a Class III anti-CEA antibody. Further, none of the cited prior art references, alone or in combination, provide any rationale for doing so.

CONCLUSION

In view of the above remarks and amendments, Applicant respectfully submit that this application is in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to telephone the undersigned at the number listed below if the Examiner believes such would be helpful in advancing the application to issue.

If any additional fees are required for the filing of this paper, Applicant authorize the Commissioner to charge any deficiency to Deposit Account No. 08-1641.

Respectfully submitted,

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